

## RECURRENT LYMPHOGRANULOMA VENEREUM\*†

### REPORT OF A CASE

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Lymphogranuloma venereum occurs infrequently in Great Britain; during the years 1952–62 a total of 906 cases was reported from the venereal diseases clinics in England and Wales (King, 1964). With the exception of two of the six cases reported by Galbraith, Graham-Stewart, and Nicol (1957) and one of the 61 cases reported by Erskine (1958), most if not all of these infections were acquired abroad, the majority occurring in British and foreign seafarers (Alergant, 1957, 1961; Erskine, 1958; Fluker, 1963). Thus it is rarely possible in any one centre to follow up a patient for a long time after his apparent cure. The case reported here shows a number of unusual features and these were observed over a period of no less than 12 years.

#### Case Report

In November, 1954, an Englishman aged 20 years attended the Venereal Diseases Clinic in Bradford. He had recently been released from the army and produced an Army Form (Med. 18) issued at a Military Hospital in Hong Kong which recorded that in June, 1954, he had received five injections of streptomycin combined with sulphonamides by mouth for the treatment of a non-specific urethritis. There was a note that he had previously been treated for non-specific urethritis in December, 1953. This infection had developed one week after a visit to a Hong Kong brothel. The patient stated that on that occasion he had been kept in hospital for 3 weeks, because a few days after the urethral discharge had cleared a painless lump had appeared in the left groin; after an unsuccessful attempt at aspiration he had been given streptomycin injections and sulphonamide tablets for 15 days.

When he was seen in Bradford in 1954, the patient had no symptoms and there was no evidence of a genital lesion or of enlargement of inguinal glands; the urine was clear, the prostate felt normal, and serum tests for syphilis gave negative results. He was discharged from the clinic.

In May, 1957, 2½ years later, the patient was again referred to the clinic because a painless swelling had re-appeared in the same area of the left groin. One medial lymph node of the lower left inguinal group was

found to be enlarged and slightly tender; the overlying skin was not affected, there was no fever, and findings at general physical examination were otherwise within normal limits. A Frei test produced a papule 10 mm. in diameter within 48 hours and central necrosis began on the 5th day, causing an ulcer (Fig. 1) which took 8 days to heal.

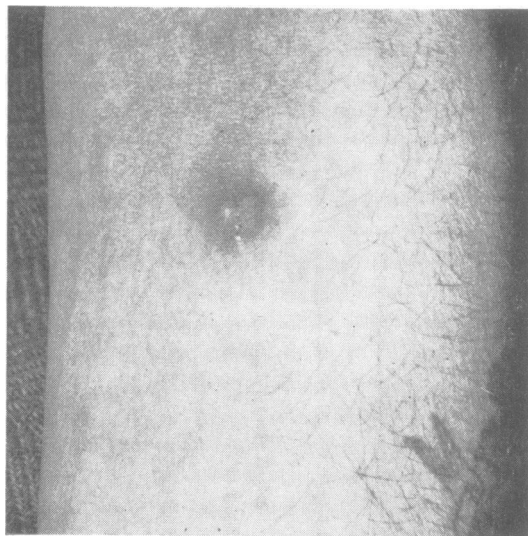


FIG. 1.—Frei test on eighth day (May, 1957).

The complement-fixation test for lymphogranuloma venereum (LGVCF) was positive at a serum dilution of 1 in 1024; the blood picture was normal and the ESR was 2 mm. in the first hour (Westergren); the total serum proteins were 8.6 g. per 100 ml. with a relative increase of globulins to 3.7 g. Serological tests for syphilis gave negative results.

On admission to hospital he began a course of oxytetracycline 500 mg. by mouth every 6 hours which was continued for 10 days; on leaving hospital the dosage was reduced to 250 mg. 6 hrly and continued for 5 days. He then received a total of 25 g. sulphatriad given in divided doses over a 10-day period. The enlarged gland became painless but did not resolve. Two months

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later the gland was still slightly enlarged, the titre of the LGVCFT had dropped to 1 in 256, and the serum globulins were reduced to 2.4 g. per 100 ml. The patient then ceased to attend.

In September, 1961, 4½ years later, the patient was again referred to the clinic. He had married in February, 1961, and his wife was pregnant. The inguinal gland originally affected had remained enlarged but about 3 weeks before his re-attendance a painful swelling had appeared above it; oxytetracycline 250 mg. four times a day had been given for 15 days by his general practitioner. There was tender enlargement of the originally affected gland and above it one gland of the horizontal inguinal group was swollen and painful, the overlying skin being reddened and adherent. Findings elsewhere were within normal limits and there was no evidence of rectal involvement. A Frei test again caused ulceration (Fig. 2).



Fig. 2.—Frei test on fourth day (September, 1961). Note scar left by test performed in 1957.

The LGVCFT was positive at a titre of 1 in 128. The patient was re-admitted to hospital and after a 10-day course of sulphadimidine totalling 63 g. he was given Nystractin (antiviral compound 17025) 2 g. intramuscularly twice weekly for 3 weeks. During the third week he took oxytetracycline 500 mg. by mouth every 6 hours to a total of 14 g. Treatment was discontinued when the white cell count in the blood fell to 3,200 per c.mm. Meanwhile the supra-inguinal bubo had resolved after previous softening; aspirated pus yielded no bacterial growth. He was discharged from hospital.

By December, 1961, the infra-inguinal gland had again become painful and another supra-inguinal bubo had developed. Further courses of tetracycline and sulphonamides were given, and 4 ml. sterile pus were aspirated from the supra-inguinal bubo.

In February, 1962, he was re-admitted to hospital because the femoral group of glands had become affected. One gland of this group softened and a discharging sinus formed and from another gland 10 ml. pus were aspirated.

Daily intramuscular injections of 200 mg. oxytetracycline were given to a total of 1.4 g., but there was little effect. The aspirated pus yielded no growth of pyogenic organisms and attempted isolation of a virus by inoculation of the yolk sac of embryonated eggs gave negative results after five passages. The titre of the LGVCFT had risen to 1 in 1024. It was then decided to treat the patient with penicillin. He was given procaine penicillin 600,000 units intramuscularly daily together with ampicillin 500 mg. three times daily orally; the glands resolved, the sinuses healed, and all activity ceased within a fortnight of beginning this treatment which was continued to a total of 28 days. Throughout this stay in hospital the patient's general condition was good, temperature normal, ESR not raised, and electrophoretic pattern of serum proteins showed only a slight increase in the globulin fraction.

The patient was followed until December, 1966. The electrophoretic pattern was normal in July, 1962. A Frei test was performed in April, 1963, and was again very strongly positive. The LGVCF test was positive at 1 in 1024 in 1963, at 1 in 512 in 1964, and at 1 in 256 in 1965 and 1966. At clinical examination in December, 1966, there were scars of Frei tests on the left forearm, areas of discoloured and hyperpigmented skin in the left inguinocrural region, and a lentil-sized hard painless nodule, a remnant of the lymphatic gland originally involved, could be felt in the left groin. There was no evidence of rectal stricture.

The patient's wife was tested in September, 1961, January, 1962, and January, 1963, and on all occasions the Frei and LGVCF tests were negative. She gave birth to a healthy son in October, 1961, and has had two more children since.

### Discussion

There is little doubt that the patient acquired lymphogranuloma venereum in Hong Kong in 1953. The urethral discharge which appeared a week after sexual exposure was most probably due to an intra-urethral primary lesion. The history of a swelling in the groin and of its attempted puncture in a military hospital suggests that syphilis was suspected and the real nature of the disorder unrecognized. The treatment which he then received for non-specific urethritis may have produced a carrier state, which according to Rake (1948) is not an infrequent result of sulphonamide therapy.

It is unusual that a relapse which occurred 3½ years after infection should have been followed by a second period of latency after treatment with oxytetracycline, and that the second relapse 8 years after infection should have presented clinical manifestations of the early stage of the inguinal syndrome of lymphogranuloma venereum. It is interesting that, in spite of the very strong specific reactions, the non-specific body responses usually associated with an active stage of the disease, such as acceleration of

erythrocyte sedimentation rate and hyperglobulinaemia to the degree of inversion of the albumin/globulin ratio (Canizares, 1954) were absent and that there was no systemic disturbance at any stage.

Greaves and Taggart (1953) provided proof that patients with latent lymphogranuloma venereum might transmit the disease to their sexual partners; King, Barwell, and Catterall (1956) presumed to be infectious the 23 patients (2 per cent. of those examined) whom on routine examination by intradermal Frei and complement-fixation tests they found to be suffering from lymphogranuloma venereum. It is therefore noteworthy that the patient reviewed here did not infect his newly-married wife before and during his severe second relapse.

Considering that penicillin is generally regarded as of no use in lymphogranuloma venereum (King, 1964; Willcox, 1964), the response to penicillin was remarkable. It must be said, however, that early clinical reports were equivocal; for example, Willcox (1946, 1950, 1953) found penicillin was frequently effective in this disease in the Gold Coast, while Greenblatt, Wammock, Chen, Dienst, and West (1950) considered it to be as ineffective as streptomycin. In laboratory studies, Hamre and Rake (1947) noted that penicillin in high concentrations either inhibited the growth of the virus (penicillin G and K) or was viricidal (penicillin F) and, though it was the least efficient in suppressing experimental infection in chick embryos and mice, of the four antibiotics tried by Hurst, Peters, and Melvin (1950), it eradicated the infection in a higher proportion of cases than did the other antibiotics. Barwell and King (1962) suggested that when other, usually effective, drugs had failed, it might be worth while to try high doses of penicillin as offering somewhat better chances of radical cure. It may well be that the newer penicillins, in particular ampicillin, are effective in lymphogranuloma venereum. On the other hand, there is no valid criterion of cure in this disease and, in view of the slow serological regression, it is impossible to be sure that the infection has been eradicated in this case.

### Summary

A case of lymphogranuloma venereum in which active relapses occurred 3½ and 8 years after infection is described. During the relapses the LGVCF tests were positive at a titre of 1 in 1024 and the intradermal Frei tests resulted in ulcerations which have left permanent scars. The second relapse had all the clinical features of the early stage of the inguinal adenitis syndrome. Repeated courses of oxy- and chlortetracycline, sulphonamides, and Nystractin failed to arrest the progress of the disease; rapid

regression of lesions and apparent cure were attained with procaine penicillin combined with ampicillin. Unusual features of the case are discussed.

I am grateful to Prof. C. F. Barwell and Mr A. J. King of the London Hospital for their interest in this case and for suggesting the use of penicillin. Prof. Barwell performed the virological investigation and the complement-fixation tests for lymphogranuloma venereum in 1962 and subsequent years. In 1957 and 1961 the tests were performed by Dr L. A. Little at the Wakefield Public Health Laboratory.

### REFERENCES

- Alergant, C. D. (1957). *Brit. J. vener. Dis.*, **33**, 47.  
 — (1961). *Ibid.*, **37**, 270.  
 Barwell, C. F., and King, A. J. (1962). Personal communication.  
 Canizares, O. (1954). "Modern Diagnosis and Treatment of the Minor Venereal Diseases", Chap. 3. Thomas, Springfield, Ill.  
 Erskine, D. (1958). *Brit. J. vener. Dis.*, **43**, 163.  
 Fluker, J. L. (1963). *Ibid.*, **39**, 24.  
 Galbraith, H.-J. B., Graham-Stewart, C. W., and Nicol, C. S. (1957). *Brit. med. J.*, **2**, 1402.  
 Greaves, A. B., and Taggart, S. R. (1953). *Amer. J. Syph.*, **37**, 273.  
 Greenblatt, R. B., Wammock, V. S., Chen, C. H., Dienst, R. B., and West, R. M. (1950). *J. vener. Dis. Inform.*, **31**, 45.  
 Hamre, D., and Rake, G. (1947). *J. infect. Dis.*, **81**, 175.  
 Hurst, E. W., Peters, J. M., and Melvin, P. (1950). *Brit. J. Pharmacol.*, **5**, 611.  
 King, A. (1964). "Recent Advances in Venereology", Chap. 11, pp. 304-333. Churchill, London.  
 —, Barwell, C. F., and Catterall, R. D. (1956). *Brit. J. vener. Dis.*, **32**, 209.  
 Rake, G. (1948). *Amer. J. trop. Med.*, **28**, 555.  
 Willcox, R. R. (1946). *Postgrad. med. J.*, **22**, 96.  
 — (1950). *J. roy. Army med. Cps*, **94**, 126 (Quoted by Willcox, 1953).  
 — (1953). "Progress in Venereology", Chap. 3, pp. 34-42. Heinemann, London.  
 — (1964). "Textbook of Venereal Diseases and Treponematoses", 2nd ed., Chap. 3, pp. 41-53. Heinemann, London.

### Le lymphogranulome vénérien récurrent

#### RÉSUMÉ

Un cas de lymphogranulome vénérien est décrit où des rechutes marquées ont eu lieu 3 ans et demi et 8 ans après l'infection. Durant les rechutes les tests LGVCF étaient positifs à un titrage de 1 dans 1,024 et les tests Frei intradermiques ont donné des ulcérations causant des cicatrices permanentes. La deuxième rechute avait tous les signes cliniques du stade précoce du syndrome adéno-inguinal. Des séries de traitements répétés avec l'oxychlorotétracycline et la chlorotétracycline, les sulfamides et la nystractine n'avaient pas arrêté le progrès de la maladie; la régression rapide des lésions et la cure apparente ont été obtenues en employant la procaine pénicilline combinée à l'ampicilline.

Les signes peu communs de ce cas sont discutés.